

THE EFFECT OF INTERMITTENT EXPOSURE  
TO 3% CO<sub>2</sub> ON RESPIRATION

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## SUMMARY PAGE

### THE PROBLEM

To determine whether intermittent exposure to 3% CO<sub>2</sub> results in a saturation of the body with carbon dioxide and whether a compensation of the respiratory acidosis induced by carbon dioxide inhalation occurs.

### FINDINGS

Intermittent exposure of one subject for six days to increased CO<sub>2</sub> for fifteen hours produced a transient filling and emptying of CO<sub>2</sub> stores within a five-day period, leading to normal alveolar CO<sub>2</sub> levels and gas exchange data on the sixth day. An equilibrium was obtained after five days at a normal alveolar and blood CO<sub>2</sub> level in contrast to continuous exposure to 3% CO<sub>2</sub>, in which an equilibrium is obtained at an elevated blood and tissue CO<sub>2</sub> level. It is concluded therefore that intermittent exposure to 3% CO<sub>2</sub> does not lead to a prevailing saturation of the organism with CO<sub>2</sub> or a compensation of the respiratory acidosis. The ventilatory response to CO<sub>2</sub> is increased during intermittent exposure to CO<sub>2</sub>, rather than decreased as is the case in chronic hypercapnia (3% CO<sub>2</sub>).

### APPLICATIONS

These findings are of importance for submarine medical officers dealing with carbon dioxide toxicity in submarines, and for scientists interested in the effects of carbon dioxide.

### ADMINISTRATIVE INFORMATION

This investigation was conducted as a part of Bureau of Medicine and Surgery Research Work Unit M4306.02-7050B - Physiological Effects of Intermittent Exposure to Increased CO<sub>2</sub> and Lowered O<sub>2</sub> Levels. The present report is No. 1 on this Work Unit. The manuscript was approved for publication on 20 March 1970 and designated as Submarine Medical Research Laboratory Report No. 618.

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## ABSTRACT

An investigation was conducted to determine whether intermittent exposure to 3% CO<sub>2</sub> results in a saturation of the body with carbon dioxide and whether a compensation of the respiratory acidosis is induced by carbon dioxide inhalation.

One healthy male subject was exposed for six days, 15 hours daily, to a CO<sub>2</sub> concentration rising from 0 - 3% at normal oxygen concentrations of 20 - 21% O<sub>2</sub>.

Average data of physiological measurements made (A) prior to and (B) at the end of the 15-hour exposure to CO<sub>2</sub> concentration, rising linearly from 0 - 3% CO<sub>2</sub> were PA<sub>CO<sub>2</sub></sub> (A): 40.7 mm Hg; PA<sub>CO<sub>2</sub></sub> (B): 42 mm Hg; PA<sub>O<sub>2</sub></sub> (A): 100.7 mm Hg; PA<sub>O<sub>2</sub></sub> (B): 114.8 mm Hg; V<sub>E</sub>(A): 6.28 L/m; V<sub>E</sub> (B): 12.09 L/m.

PA<sub>CO<sub>2</sub></sub> determined at the end of the nine-hour air breathing rose from the third day on to reach, at the fifth day, a peak higher than the corresponding value following 15 hours of CO<sub>2</sub> inhalation. During the sixth day of intermittent exposure to CO<sub>2</sub>, PA<sub>CO<sub>2</sub></sub> on air returned to control values. This finding indicates that after three days the nine-hour period of air breathing was insufficient to eliminate the CO<sub>2</sub> accumulated during the 15-hour period of CO<sub>2</sub> breathing.

Ventilatory response to 5% CO<sub>2</sub> was increased during intermittent exposure to CO<sub>2</sub> and the slope of the CO<sub>2</sub> tolerance curve was also increased.



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## INTRODUCTION

Compensation of the respiratory acidosis produced by inhalation of moderate CO<sub>2</sub> concentration (3% CO<sub>2</sub> = 21 mm Hg) has been found to require approximately five days in man<sup>2, 3, 4</sup>. During this adaptation to CO<sub>2</sub>, a reduction in the ventilatory response occurs. Studies on intermittent exposure to 3% CO<sub>2</sub> have not been reported. The purpose of this investigation was to determine whether a compensation of the respiratory acidosis is reached during intermittent exposure to 3% CO<sub>2</sub>.

## METHODS

Resting respiratory minute volume ( $\dot{V}_E$ ), oxygen consumption ( $\dot{V}_{O_2}$ ) carbon dioxide excretion ( $\dot{V}_{CO_2}$ ), alveolar carbon dioxide and oxygen tensions (PACO<sub>2</sub>) and (PAO<sub>2</sub>) were measured twice daily, between 8-9 AM and 10:30-11:00 PM. Average end tidal gas samples were collected with a Rahn sampler and analyzed with a Beckman LB-1 infrared CO<sub>2</sub> meter and a Servomex O<sub>2</sub> meter. Mixed expired gas was collected in a Douglas bag for the last six minutes of the ten-minute test period. Volume measurements were made with a dry gas meter.

The respiratory rate was determined with a Yellow Springs thermistor inserted at the side of the mouthpiece.

CO<sub>2</sub> tolerance tests consisting of ten-minute inhalation of 5% CO<sub>2</sub> in 21%

O<sub>2</sub> were carried out on six occasions, twice daily following the measurement of resting ventilation.

## RESULTS

The effect of intermittent exposure to CO<sub>2</sub> on pulmonary ventilation and alveolar gas tensions is shown in Figure 1 and Table I. Respiratory minute volume increased to twice the resting ventilation on air at the end of the 15-hour exposure to rising CO<sub>2</sub> concentration reaching 3% CO<sub>2</sub> at the time the measurement was made. Alveolar CO<sub>2</sub> tension rose from 40.7 mm Hg to 42.4 mm Hg while the alveolar O<sub>2</sub> tension increased from 100.7 mm Hg to 114.8 mm Hg. All the values obtained after nine hours of air breathing remained at control levels with the exception of the alveolar CO<sub>2</sub> tension, which rose on the fourth and fifth day, reaching a peak which was

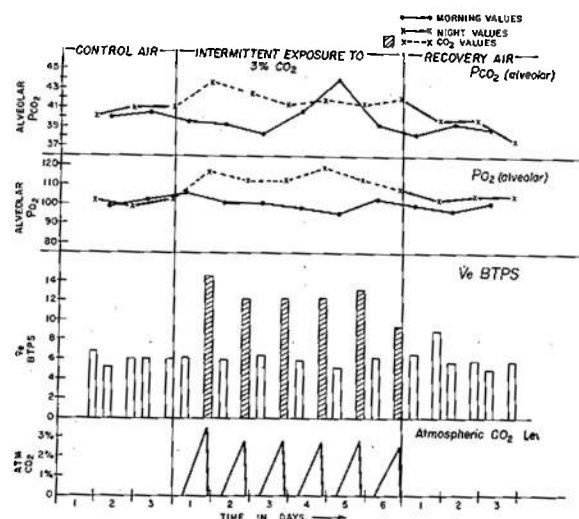


Figure 1

Table I. Effect of Intermittent Exposure to 3% CO<sub>2</sub> on Respiratory Minute Volume ( $\dot{V}_E$ ), Alveolar Carbon Dioxide (P<sub>A</sub>CO<sub>2</sub>) and Oxygen Tension (P<sub>A</sub>O<sub>2</sub>)

Condition		$\dot{V}_E$ BTPS	P <sub>A</sub> CO <sub>2</sub>	P <sub>A</sub> O <sub>2</sub>
		L/min	mm Hg	mm Hg
Control 8 AM	Mean	5.68	40.7	101.0
	N	2	2	2
Control 11 PM	Mean	6.22	42.4	100.7
	SEM	.27	1.2	1.2
	N	3	3	3
Experi- mental 9 hours on air	Mean	5.99	40.4	101.8
	SEM	.17	.9	1.4
	N	6	6	6
Exposure 15 hours on CO <sub>2</sub> (0-3%CO <sub>2</sub> ) 11 PM	Mean	12.35 **	42.4	114.8 **
	SEM	.70	.4	1.5
	N	6	6	6
Recovery on air 8 AM	Mean	5.79	39.0	100.8
	SEM	.47	.2	1.2
	N	3	3	3
Recovery on air 11 PM	Mean	6.59	38.8	105.0
	SEM	.70	1.4	.7
	N	3	3	3

\* Statistically different from control levels.

\*\* Statistically significant difference between data obtained after 9 hours on air (8AM) and 15 hours on CO<sub>2</sub> (0-3% CO<sub>2</sub>) at 11 PM

even higher than the corresponding value on CO<sub>2</sub> breathing. This indicates that the nine-hour period of air breathing was, after three days, not sufficient to eliminate the previously accumulated CO<sub>2</sub>.

Data on oxygen consumption, CO<sub>2</sub> excretion and respiratory exchange ratio are presented in Table II and daily changes in Figure 2. CO<sub>2</sub> excretion is consistently elevated during CO<sub>2</sub> breathing while the oxygen consumption does not change significantly. It should be noted that the oxygen consumption during air breathing tends to decline, a condition which leads to an increase of the respiratory exchange ratio during the fourth and fifth day corresponding to the rise in alveolar CO<sub>2</sub> tension. The subsequent return of the respiratory exchange ratio to near normal values on the sixth day of intermittent CO<sub>2</sub> exposure, which is paralleled by the fall in alveolar CO<sub>2</sub> tension, suggests that the more rapidly exchanging CO<sub>2</sub> stores of the body were able to give up the previously accumulated CO<sub>2</sub> during two air breathing periods of 18 hours.

The ventilatory response to inhalation of 5% CO<sub>2</sub> increased during the sixth day of intermittent exposure to 3% CO<sub>2</sub>, as shown in Table III.  $P_{A\text{CO}_2}$  tended to decrease and  $P_{A\text{O}_2}$  to rise.

The slope of CO<sub>2</sub> tolerance curves increased during the intermittent exposure to CO<sub>2</sub> and during the recovery period on air.

Intermittent exposure to 3% CO<sub>2</sub> had effects on lung functions (Table IV). Vital capacity was found decreased at

the end of the 15-hour period of CO<sub>2</sub> exposure and also in the morning after a 9-hour period of air breathing. The same is true for the expiratory reserve volume, while inspiratory capacity was unaffected. The maximum expiratory flow rates (MEFR) did decrease, not only during the experimental period, but remained below control levels during the recovery period on air, in contrast to the maximal inspiratory flow rates (MIFR) which did not change.

## DISCUSSION

The experimental design in this study of intermittent exposure to CO<sub>2</sub> required the scheduling of measurements at 8 AM, prior to eating, and 11 PM, three hours after supper. Diurnal variations of physiological functions therefore influence the measurements and comparisons have to be made of corresponding time periods.

Moreover, the alternating periods of air breathing and CO<sub>2</sub> breathing during intermittent exposure exhibit both CO<sub>2</sub> effects. In the former, CO<sub>2</sub> accumulates during the fourth and fifth day while the latter shows a direct effect of CO<sub>2</sub> inhalation.

In the recovery period on air, alveolar and blood carbon dioxide quickly return to control values after eight hours of air breathing and remain at this level but the main carbon dioxide elimination occurs on the second day of recovery, as indicated in a large excretion of urine bicarbonate<sup>6</sup>. This suggests that metabolic effects of CO<sub>2</sub> are still present at a

Table II. Effect of Intermittent Exposure to 3% CO<sub>2</sub> on Carbon Dioxide Excretion ( $\dot{V}_{CO_2}$ ), Oxygen Consumption ( $\dot{V}_{O_2}$ ) and Respiratory Exchange Ratio (R)

Condition		$\dot{V}_{CO_2}$	$\dot{V}_{O_2}$	R
Control 8 AM	Mean	186.5	236.0	.79
	N	2	2	2
Control 11 PM	Mean	205.7	252.7	.81
	SEM	6.2	8.2	.01
	N	3	3	3
Experi- mental 9 Hours on air 8 AM	Mean	189.2	223.8	.86
	SEM	3.0	10.9	.04
	N	6	6	6
Exposure 15 hours on CO <sub>2</sub> (0-3% CO <sub>2</sub> ) 11 PM	Mean	228.2 **	248.5	.92 *
	SEM	7.8	11.1	.02
	N	6	6	6
Recovery on air 8 AM	Mean	183.3	236.3	.78
	SEM	12.0	12.2	.02
	N	3	3	3

\* Statistically significantly different from control levels at the 5% level.

\*\* Statistically significant difference between data obtained after 9 hours on air (8 AM) and 15 hours on CO<sub>2</sub> (0-3% CO<sub>2</sub>) at 11 PM at the 5% level and better



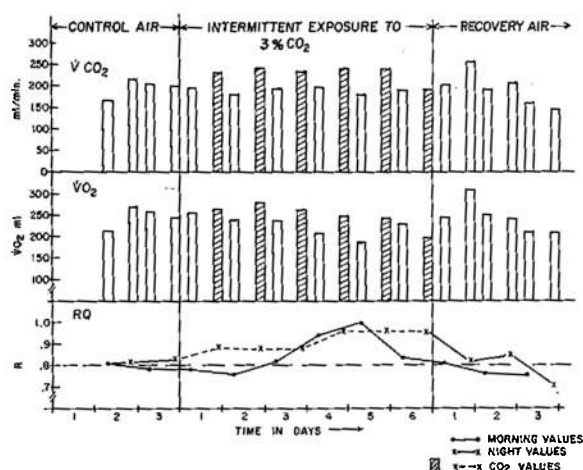


Figure 2

time of the recovery period when alveolar and blood  $\text{CO}_2$  tensions are essentially normal.

The preliminary study on intermittent exposure to 3%  $\text{CO}_2$  produced two essential findings which are in contrast to the well known effects of chronic exposure to 3%  $\text{CO}_2$ :

1. A transient filling and emptying of  $\text{CO}_2$  stores of the body within a five-day period resulting in normal alveolar  $\text{CO}_2$  tensions and pulmonary gas exchange data on the day of intermittent exposure. This indicates that pulmonary and renal regulations<sup>6</sup> stimulated by accumulated  $\text{CO}_2$ , are adequate to attain an equilibrium at a normal  $\text{CO}_2$  level rather than at an elevated  $\text{CO}_2$  level, as in chronic hypercapnia. One can, therefore, not speak about a compensation of a respiratory acidosis.

It is interesting to note one similarity between intermittent and chronic

Table III. Effect of Intermittent Exposure to  $\text{CO}_2$  For Six Days on Ventilatory Response to 5%  $\text{CO}_2$ , Alveolar Gas Tension and Slope of  $\text{CO}_2$  Tolerance Curves

Conditions		$\dot{V}_E$ L/m BTPS	$P_{\text{ACO}_2}$ mm Hg	$P_{\text{AO}_2}$ mm Hg	Slope of $\text{CO}_2$ toler- ance curves
Control	Mean	19.58	49.5	132.7	.365
	Range	(18.9-20.3)	(49.0-50.0)	(131.7-133.7)	(.31-.42)
	N	2	2	2	2
Inter- mittent $\text{CO}_2$ period of 6 days	Mean	24.37	47.04	136.7	.493
	S. E.	(1.64)	(0.59)	(.75)	(.031)
	N	6	6	6	6
Recovery on air	Mean	21.62	45.06	135.1	.520
	S. F.	(.80)	(.33)	(1.77)	(.042)
	N	4	4	4	4

Table IV. Effect of Intermittent Exposure to 3% CO<sub>2</sub> on Lung Functions, Vital Capacity (VC), Inspiratory Capacity (IC), Expiratory Reserve Volume (ERV), Maximum Expiratory Flow Rate (MEFR), Maximum Inspiratory Flow Rate (MIFR), Maximum Voluntary Ventilation (MVV)

Condition		VC liters	IC liters	ERV liters	MEFR L/sec	MIFR L/sec	MVV L/min
Control 8 AM	Mean	5.83	3.61	2.22	14.05	12.66	198
	SEM	.08	.01	.08	.15	.28	16
	N	3	3	3	3	3	3
Control 11 PM	Mean	5.87	3.95	1.93	13.51	12.18	210
	SEM	.07	.10	.03	.34	.54	12
	N	3	3	3	3	3	3
Experi- mental on air 8 AM	Mean	5.62	3.68	1.94*	12.90*	12.74	225
	SEM	.05	.04	.04	.27	.15	3
	N	6	6	6	6	6	6
Experi- mental on 3% CO <sub>2</sub> 11 PM	Mean	5.73	3.97	1.77	12.94	12.82	225
	SEM	.03	.07	.07	.16	.20	5
	N	6	6	6	6	6	6
Recovery 8 AM	Mean	5.67	3.91*	1.76*	12.56*	12.55	244
	SEM	.06	.07	.01	.11	.27	3
	N	3	3	3	3	3	3
Recovery 11 PM	Mean	5.80	3.97	1.82	12.45	12.96*	245*
	SEM	.01	.14	.01	.48	.23	2
	N	3	3	3	3	3	3

\* Statistically significant difference from control levels at the 5% confidence level.

exposure to 3% CO<sub>2</sub>. The same time period of five days is required to come back to control levels in the first case and reach a compensation of the respiratory acidosis in the second case.

2. Findings of an increased ventilatory response to CO<sub>2</sub> and increased slope of the CO<sub>2</sub> response curve during intermittent exposure to 3% CO<sub>2</sub> are

opposite to the depression of ventilatory response and decrease in slope observed in chronic exposure to 3% CO<sub>2</sub><sup>3</sup>.

The decrease in vital capacity observed during the experimental period, both during air breathing and during CO<sub>2</sub> breathing, is associated with a decrease in expiratory reserve

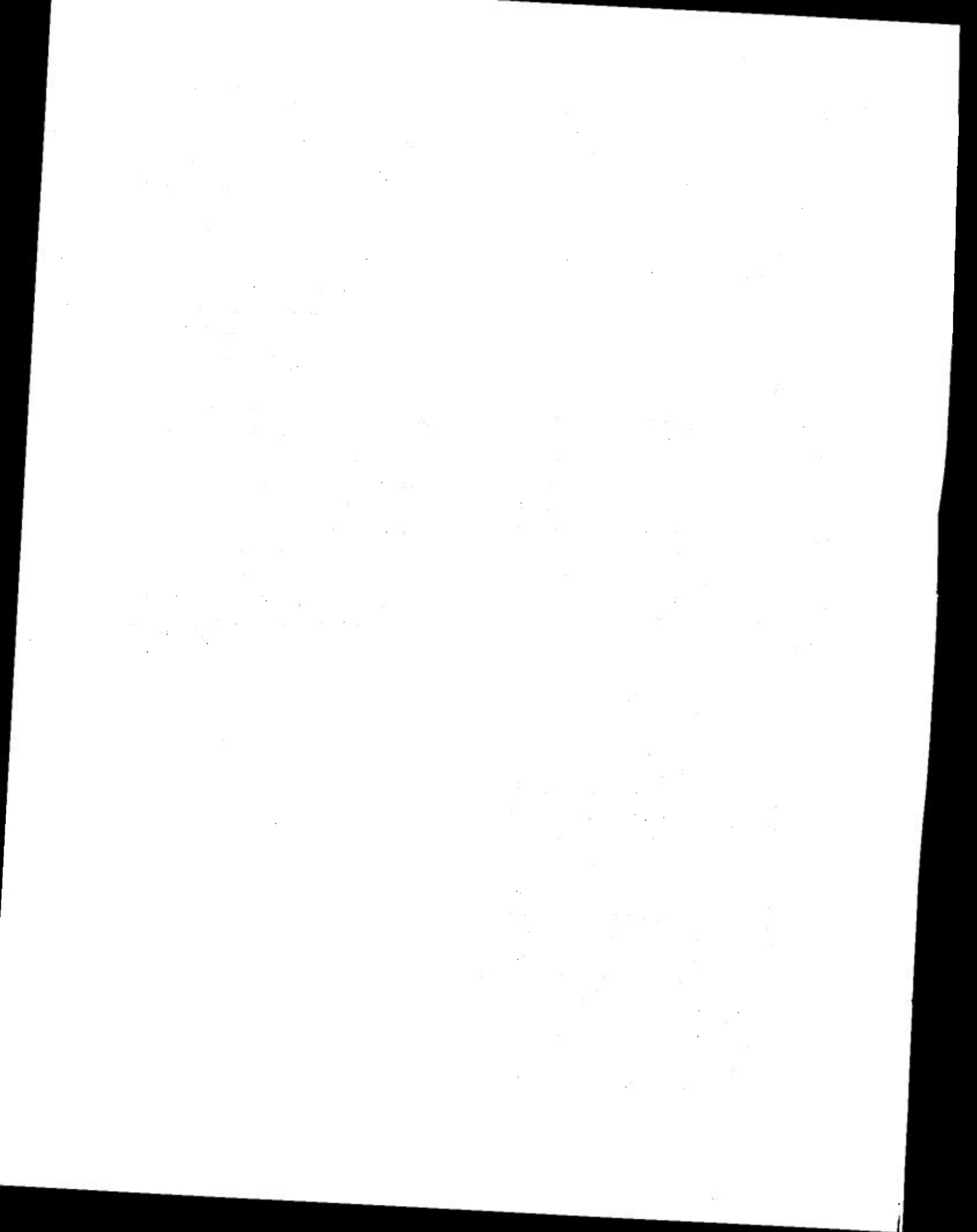
volume which might be caused by blood volume shifts into the thorax, due to CO<sub>2</sub> inhalation or the slow accumulation of CO<sub>2</sub> during the air breathing period.

The decrease in MEFR of approximately one liter/second, observed during both experimental periods and during the third day of recovery period, suggests a CO<sub>2</sub> induced increase in airway resistance.

Hypercapnia induced by inhalation of 7% CO<sub>2</sub> has been found to increase airway resistance<sup>7</sup> but ten minute exposure to lower CO<sub>2</sub> concentrations (4-10%) did not change airway resistance<sup>1</sup>. Our findings seem to suggest that prolonged exposure of 15 hours to a CO<sub>2</sub> concentration rising to 3% CO<sub>2</sub> has an effect on airway resistance. More investigations on a larger group of subjects are needed to clarify this effect of CO<sub>2</sub>.

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13. ABSTRACT <p>One healthy male subject was exposed for six days, 15 hours daily, to a CO<sub>2</sub> concentration rising from 0 - 3% CO<sub>2</sub> at normal oxygen concentrations of 20 - 21% O<sub>2</sub></p> <p>Average data of physiological measurements made (A) prior to and (B) at the end of the 15-hour exposure to CO<sub>2</sub> concentration, rising linearly from 0 - 3% CO<sub>2</sub> were <math>P_{A_{CO_2}}(A)</math>: 40.7 mm Hg; <math>P_{A_{CO_2}}(B)</math>: 42 mm Hg; <math>P_{A_{O_2}}(A)</math>: 100.7 mm Hg; <math>P_{A_{O_2}}(B)</math>: 114.8 mm Hg; <math>\dot{V}_E(A)</math>: 6.28 L/m; <math>\dot{V}_E(B)</math>: 12.09 L/m.</p> <p><math>P_{A_{CO_2}}</math> determined at the end of the nine-hour air breathing rose from the third day on to reach, at the fifth day, a peak higher than the corresponding value following 15 hours of CO<sub>2</sub> inhalation. During the sixth day of intermittent exposure to CO<sub>2</sub>, <math>P_{A_{O_2}}</math> on air returned to control values. This finding indicates that after three days the nine-hour period of air breathing was insufficient to eliminate the CO<sub>2</sub> accumulated during the 15-hour period of CO<sub>2</sub> breathing.</p> <p>Ventilatory response to 5% CO<sub>2</sub> was increased during intermittent exposure to CO<sub>2</sub> and the slope of the CO<sub>2</sub> tolerance curve was also increased.</p>		

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